REMARKS

Claims 7-22 and 24 were pending in the instant application. The specification has been amended to include sequence identity numbers for sequences cited in the specification. Claims 8, 10, 11, 20 and 24 have been cancelled without prejudice. Claims 7, 9, 12-17 and 21 have been amended in order to claim more fully and distinctly the invention. New claims 25-26 have been added. Accordingly, claims 7, 9, 12-19, 21-22, and 25-26 are currently pending in the present application. Support for the amended specification and claims can be found throughout the specification and claims as originally filed. Specifically, support for the amended specification may be found at least at page 22, line 16 though page 23, line1, page 28, Table 4, page 31, Table 5, page 33, lines 12-14, page 34, Table 6, page 36, Table 7, page 38, Table 8, page 40, Table 10, page 46, Table 11, page 48, Table 12 and page 52, Table 13. Support for amended claims 7, 9, 12-17, 21 and 25-26 may be found in the instant specification at least, for example, at page 3, line 13 through page 4, line 8 and page 11, Table 2. Support for added claims 25-26 may be found in the instant specification at least, for example, at page 13, line 27 through page 14, line 13. No new matter has been added.

Attached hereto is Appendix A, captioned "VERSION WITH MARKINGS TO SHOW CHANGES MADE." The attached Appendix includes a marked-up version of the changes made to the specification by the current amendment. Also attached hereto is APPENDIX B, including the full set of claims that are currently pending.

Amendment to the claims is not to be construed as acquiescence to any of the rejections set forth in the instant Office Action, and was done solely to expedite prosecution of the instant application. Applicants reserve the right to pursue the claims as originally filed, or similar claims, in this or one or more patent applications.

Election/Restriction

The Office Action states that "claim 24 is independent and distinct from Group I," which is drawn to a protein comprising an amino acid sequence as set forth in SEQ ID NO:1, the DNA encoding this protein, a vector and a host cell. Based on the subsequent statement in the Office Action that claims 7-22 and 24 are under consideration,

Applicants have concluded that the Office Action contains a typographical error, *i.e.*, that claim **23** not claim **24** has been withdrawn from consideration. Accordingly, Applicants have cancelled claim 23 as being drawn to a non-elected invention. If this assumption is incorrect, further clarification is requested.

Specification

The specification was objected to because the sequences appearing within the text are not identifed by SEQ ID NOs. Accordingly, the specification has been amended to include sequence identifiers where appropriate, and a substitute sequence listing in hard copy and on disk is being filed concurrently herewith.

Claim Rejections Under 35 U.S.C. §101

Claims 7-22 and 24 stand rejected under 35 U.S.C. §101 on the ground that a specific asserted utility or a substantial utility does not support the claimed invention. Applicants respectfully disagree and traverse the forgoing rejection for the following reasons.

Claims 8, 10, 11, 20 and 24 have been cancelled, rendering the rejection moot with respect to these claims. With respect to the presently pending claims 7, 9, 12-19, 21-22 and 25-26, it is Applicants' position that a specific and substantial utility for the claimed invention is clearly set forth in the instant specification and the knowledge in the art at the time of Applicants' invention.

Applicants disclose in the instant specification a full-length cDNA ("clone HP01263") which contains an open reading frame encoding the polypeptide of SEQ ID NO:1. Further characterization of this clone was performed through the use of available computer programs (see, *e.g.*, the instant specification at 21, lines 19-26 and page 27, lines 21-25). Specifically, protein databases such as SWISS-PROT as well as hydrophobicity/hydrophicility profiles as obtained using the well-known Kyte-Doolittle methods were used to search for sequence homology and additional protein structural characteristics (*id.*). This approach is in accordance with Doerst *et al.*, as cited by the Examiner, which states that "[c]omputer analysis of genome sequences is currently one

of the *essential* steps for obtaining functional and structural information about the respective gene products" (page 248, first column, first paragraph).

Applicants assert in the instant specification that the protein has a significant degree of homology to α-2-HS-glycoprotein (SWISS-PROT Accession number P02765) (see, *e.g.*, page 27, lines 21-25), a member of the fetuin family of proteins. Based on this homology, Applicants assert that clone HP01263 shares the activities of these molecules.

The fetuin family of proteins encompasses a series of tightly related orthologous plasma proteins involved in fetal development. These proteins, which are well known in the art, have been ascribed many functions and are considered key proteins in several metabolic pathways. Specifically, these proteins are known to be involved in osteogenesis and bone resorption, the modulation of insulin-driven and kinase-mediated signal transduction pathways and a key partner in the recovery step of an acute-phase response to systemic inflammation. These activities are important for a number of biological functions, including tissue growth activity, receptor-ligand activity and anti-inflammatory activity.

Applicants assert that novel molecules of the present invention can be used, for example, as modulators of tissue growth activity, i.e. for inducing bone growth (see, *e.g.*, page 72, line 20 through page 73, line 6), as modulators of receptor/ligand activity, i.e. through regulating receptor kinases and/or receptor phosphatases and their ligands (see, *e.g.*, page 79, lines 14-25) or as modulators of anti-inflammatory activity, i.e. by stimulating or suppressing production of other factors which more directly inhibit or promote an inflammatory response (se, *e.g.*, page 80, lines 20-25).

The specificity of the asserted utilities is based on the fact that the polypeptide of the present invention belongs to the fetuin protein family, a family sharing structural and functional characteristics that are not shared by other non-fetuin proteins. In particular, fetuins are known to play an important role during fetal development and have been named as key players in several metabolic pathways, including osteogenesis and bone resorption, insulin-driven and kinase-mediated signal transduction pathways and the recovery phase of acute phase responses. This activity is important for a number of biological functions, including tissue growth activity, receptor-ligand activity, and anti-inflammatory activity. Applicants respectively assert that these activities are specific to

the fetuin family of proteins and are not shared by all other protein-encoded nucleic acid molecules.

Moreover, no evidence has been made of record that Applicants' assertions regarding the activity and/or utility of SEQ ID NO:1 polypeptides as modulators of tissue growth activity, receptor-ligand activity or anti-inflammatory activity would not be considered credible to one of skill in the art. As stated in the Federal Register (Vol. 66, No. 4, page 1096):

> when a patent application claiming a nucleic acid asserts a specific, substantial and credible utility, and *bases the assertion upon homology* to existing nucleic acids or proteins having an accepted utility, the asserted utility *must be accepted* by the examiner unless the Office has sufficient evidence or sound scientific reasoning to rebut such an assertion. "[A] 'rigorous correlation' need not be shown in order to establish practical utility; 'reasonable correlation' is sufficient," *Fujikawa v. Wattanasin,* 93 F.3d 1559, 1565, 39 USPQ2d 1895, 1900 (Fed. Cir. 1996). The Office will take into account both the nature and degree of homology [emphasis added].

The instant application teaches a specific and substantial biological function for the SEQ ID NO:1 polypeptides of the invention. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of the claims under 35 U.S.C. §101.

Claim Rejections Under 35 U.S.C. §112, first paragraph

Claims 7-22 and 24 were rejected under 35 U.S.C. §112, first paragraph. Specifically, the Office Action states that "[s]ince the claimed invention is not supported by either a specific and substantial utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention." Applicants respectfully traverse.

Without acquiescing to the alleged lack of enablement in the specification as originally filed, claims 8, 10, 11, 20 and 24 have been cancelled, thus rendering the rejection moot. Applicants submit the rejection with regard to these claims is therefore obviated.

With respect to still pending claims 7, 9, 12-19, 21-22 and 25-26, Applicants would like to make the following remarks of record. As argued above, the present invention is supported by a substantial utility and a well-established utility. Specifically,

the asserted utilities are based on the fact that SEQ ID NO:1 polypeptides of the present invention belong to the fetuin family of proteins. Further, the specification is replete with teachings of how to make and/or use the present invention. For instance, the specification teaches that novel molecules of the present invention can be used, for example, as modulators of tissue growth activity, i.e. for inducing bone growth (see, *e.g.*, page 72, line 20 through page 73, line 6), as modulators of receptor/ligand activity, i.e. through regulating receptor kinases and/or receptor phosphatases and their ligands (see, *e.g.*, page 79, lines 14-25) or as modulators of anti-inflammatory activity, i.e. by stimulating or suppressing production of other factors which more directly inhibit or promote an inflammatory response (se, *e.g.*, page 80, lines 20-25). Accordingly, the polypeptide of the present invention can be used for diagnostic and therapeutic purposes for disorders which involve any of these biological activities (see, *e.g.*, the specification, at least, for example, at page 72, line 25 through page 73, line 6, page 76, lines 1-6, page 80, lines 2-13 and page 80, line 15 through page 81, line 6). Applicants respectfully submit that any experimentation that may be required to make and/or use the claimed polypeptide molecules constitutes routine, not undue, experimentation and therefore the specification clearly enables the pending claims.

Claims 10, 12-22 and 24 were further rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Without acquiescing to the alleged lack of written description in the specification as originally filed, claims 10, 20 and 24 have been cancelled , thus rendering the rejection moot as it applies to these claims. Claims 12-17 have been amended to depend from claims 7 and 9 and claim 21 has been amended to be an independent claim and claim 22 has been amended to depend from claims 7, 9 and 21, thus rendering the rejection moot as it applies to these claims. Applicants submit that the rejection with regard to these claims is therefore obviated.

Claims 8, 11-22 and 24 were also rejected under 35 U.S.C. §112, first paragraph for lack of enablement. Specifically, the Office Action states that while the specification is enabling for a protein encoded by SEQ ID NO 1, it does not enable a "nucleic acids

encoding polypeptides comprising amino acid sequences that are fragments of said sequences."

Without acquiescing to the alleged lack of enablement in the specification as originally filed, claims 8, 11, 20 and 24 have been cancelled, thus rendering the rejection moot. Claims 12-17, and 21 have been amended to no longer depend from claims 8, 11 and/or 20. Accordingly, Applicants submit that the rejection with regard to these claims is therefore obviated.

Claim Rejections Under 35 U.S.C. §112, second paragraph

Claim 12 is rejection under 35 U.S.C. §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Office Action states that claim 12 recites the term "stringent conditions" which is a conditional term and renders the claim indefinite. Without acquiescing to the alleged lack of definiteness in the specification as originally filed, claim 11 has been amended to recite, in pertinent part, "[A]n isolated nucleic acid molecule which hybridizes under stringent conditions at least as stringent as 4x SSC at 65 degrees C, or 4x SSC at 42 degrees C with 50% formamide, followed by washing at 65 degrees C on 1x SSC, to a complement of the polynucleotide having the nucleotide sequence of SEQ ID Nos:19 or 37, siad hybridizing polynucleotide having a length that is at least 25% of the length of the polynucleotide having the nucleotide sequence of SEQ ID Nos:19 or 37." Applicants submit that the rejection with regard to these claims is therefore obviated.

Claim Rejections under 35 U.S.C. §102(b)

Claims 8-22 and 24 were rejected under 35 U.S.C. §102(b) as being anticipated by Hillier *et al.* (1996). Specifically, the Office Action states that "Hillier *et al.* discloses the cloning of a nucleotide sequence which is 42.4% identical to SEQ ID NO19 of the instant application. This nucleic acid encodes a fragment of a protein that has more than 5 contiguous amino acids identical to the sequence set forth in SEQ ID NO:1."

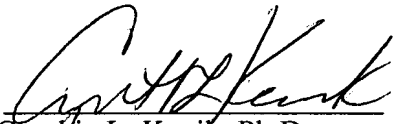
Applicants respectfully submit that the cancellation of claims 8, 10, 11, 20 and 24 without prejudice, renders the aforementioned rejection moot and request that the Examiner withdraw this §102(b) rejection as it pertains to these claims.

With respect to claims 9, 12-19 and 21-22, the Applicants respectfully traverse. The cited reference teaches a nucleic acid molecule (i.e. nucleic acid fragment or EST) which has sequence identity over a portion of the claimed nucleic acid molecules. The reference fails to teach sufficient sequence information to anticipate the claimed polynucleotides. Moreover, translation analysis utilizing the Expert Protein Analysis System (ExPASy) across all three reading frames if the EST reveals that the EST sequence fails to encode the HP01263 proteins of the present invention. Or any biologically active fragments thereof. As the cited reference fails to teach the claims polynucleotides of the invention, the invention is not anticipated by the cited reference. In view of the above, Applicants respectfully request that the Examiner withdraw the rejection of claims 8-22 and 24 under 35 U.S.C. §102(b).

CONCLUSION

If a telephone conversation with Applicants' attorney would expedite prosecution of the above-identified application, the Examiner is urged to call the undersigned at (617) 227-7400.

Respectfully submitted,
LAHIVE & COCKFIELD, LLP



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Dated: March 25, 2002